Gastric Secretion

The stomach secretes about 2.5 litres/day of acidic juice which is composed of:

1. Electrolytes: H^+, Cl, Na^+ and K^+: (pH : approximately 1.0)
2. Enzymes: Pepsin, gelatinase, lipase.
3. Mucus.
4. Intrinsic factor for absorption of vitamin B_{12}.
5. Water.

1-Acid Secretion:

It is an active process, which needs high energy. Acid is secreted by the parietal cells, which are characterised by having large number of mitochondria (for energy production) and intracellular canaliculi.

Mechanism of Acid Secretion:

The following steps occur inside the parietal cells

1. CO_2 (formed during cell metabolism or entering by blood) combines with H_2O under the effect of carbonic anhydrase enzyme to form carbonic acid.
2. Carbonic acid dissociates into HCO_3^- and H^+.
3. H^+ is actively secreted to lumen in exchange for K^+ by **H^+/K^+ ATPase pump (proton pump)**. .
4. The HCO_3^- diffuses out of the cell to blood in exchange for Cl^- ..
5. Cl^- is actively transported from the cytoplasm of parietal cells to the lumen. .
6. H_2O passes through the cell to the lumen by osmosis.

Alkaline Tide: as HCl is secreted by the parietal cells HCO_3^- is added to the gastric venous blood so the pH of the blood increases.

Stimuli of HCl secretion:

1. **Histamine**: acts via H_2 receptors. H_2 receptor stimulation increases intracellular cAMP.
2. **Acetylcholine:** acts via M_3 muscarinic receptors. M_3 receptor stimulation increases intracellular Ca^{++}.
3. **Gastrin:** it acts either directly on oxyntic cells by increasing intracellular Ca^{++} (like acetylcholine) or indirectly through stimulating the secretion of histamine from enterochromaffin-like cells (ECL cells).

Mechanism of action of HCl stimuli:

Parietal cells contain receptors for these stimuli. Binding of these stimuli with their receptors release 2nd messengers which transfer the H^+/K^+ ATPase proteins from the membranes of intracellular vesicles to the plasma membrane

Thus increasing the number of pump proteins in the plasma membranes.

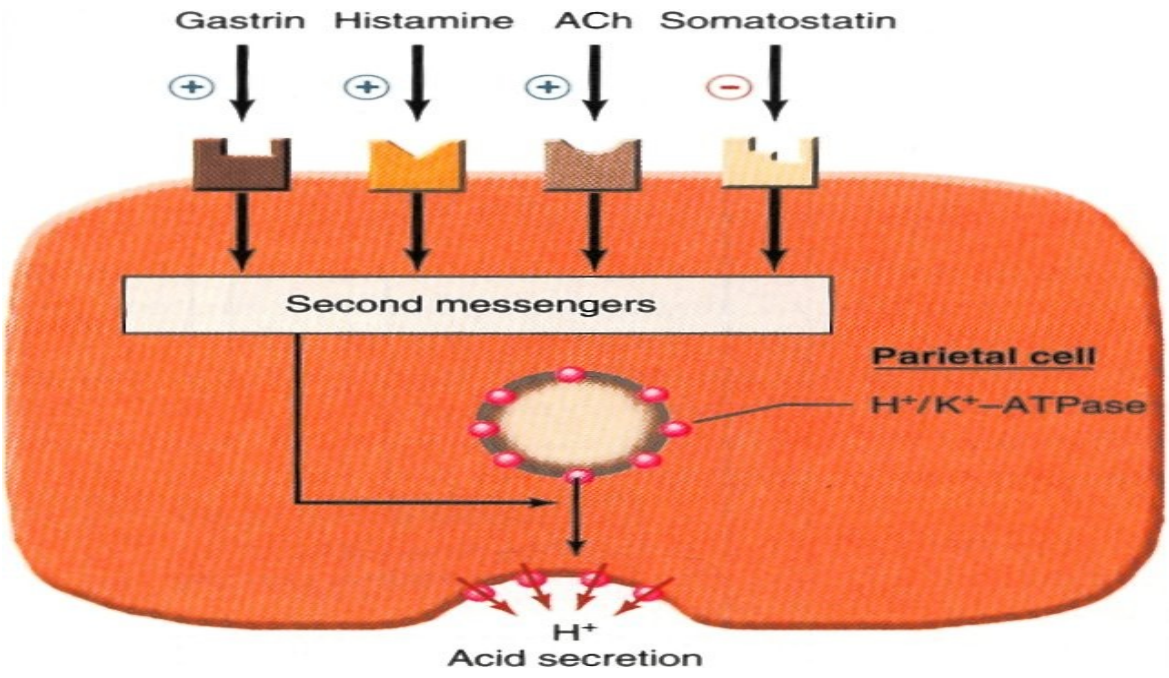

Figure (1): Mechanism of action of stimuli

Functions of HCl:

1. Maintains relative sterility of the stomach by killing ingested bacteria.
2. Dissolves food particles and changes food into "chyme".
3. Activates the inactive pepsinogen by changing it into active pepsin.
4. Provides optimum pH for the action of pepsin.
5. Helps iron and calcium absorption.
6. Stimulates the flow of bile.
7. Maintains relative sterility of the stomach by killing ingested bacteria

2-Secretion and Activation of Pepsinogen:

The pepsiongen secreted by chief (peptic) cells, is activated by HCl at pH 2 to active pepsin. This active pepsin further activates pepsinogen i.e. **positive feed back mechanism**. Pepsin digestion of proteins is incomplete to yield various peptides. Pepsin is inactivated by the alkalinity of the duodenum.

3-Secretion of Intrinsic Factor:

The intrinsic factor essential for absorption of vitamin B_{12} in the ileum is secreted by the parietal cells along with the hydrochloric acid. Therefore, when the acid-producing cells of the stomach are destroyed, which frequently occurs in chronic gastritis, the person does not only **develop achlorhydria, but also develops pernicious anemia.**

4-Secretion of mucus in the stomach:

There are two types of mucus:

-Soluble mucus:

It is secreted by mucous neck cells of the gastric glands in response to vagal stimulation. It lubricates the gastric chyme.

- Insoluble mucus:

It is secreted by the surface epithelium of the gastric body and fundus, as well as esophageal and pyloric junctions. It forms a layer 1.5mm in thickness, to protect the gastric mucosa against the mechanical friction with food, and to neutralize the corrosive effect of the acid.

Phases of Gastric Secretion:

Gastric secretion occurs in three phases: a cephalic phase, a gastric phase and an intestinal phase ***(Fig 2).***

(I) <u>The cephalic stimulatory phase</u>: (Nervous)

-Once food is thought about, or enters the mouth, both conditioned and unconditioned reflexes stimulate the dorsal nucleus of the vagus to increase secretions of HCI, pepsinogen, mucus and gastrin .

-The neurogenic signals causing the cephalic phase can originate in the cerebral cortex or in the appetite centers of the hypothalamus.

-This phase accounts for about **one third** of the gastric secretion.

-The efferent fibres for this reflex are in the vagus nerves.

<u>Vagal stimulation increases gastric secretion by:</u>

a) **Acetylcholine** which acts directly on the cells in the glands in the body and funuds.

b) Gastrin: vagal nerve endings release gastrin-releasing peptide that increases gastrin secretion.

(II) <u>The gastric stimulatory phase: (Nervous and Hormonal):</u>

Once the food enters the stomach, it excites gastric secretion by 3 mechanisms:

1- Long vagovagal reflexes like in cephalic phase.

2- Local enteric reflexes. Receptors in the wall of the stomach and the mucosa respond to stretch and chemical stimuli (mainly amino acids

and related products of digestion). The sensory fibres from the receptors enter the submucous plexus then they synapse on postganglionic parasympathetic neurons (enteric nervous system) that end on parietal cells and stimulate acid secretion.

3- Gastrin secretion.

This phase accounts for **2/3** of the total gastric secretion.

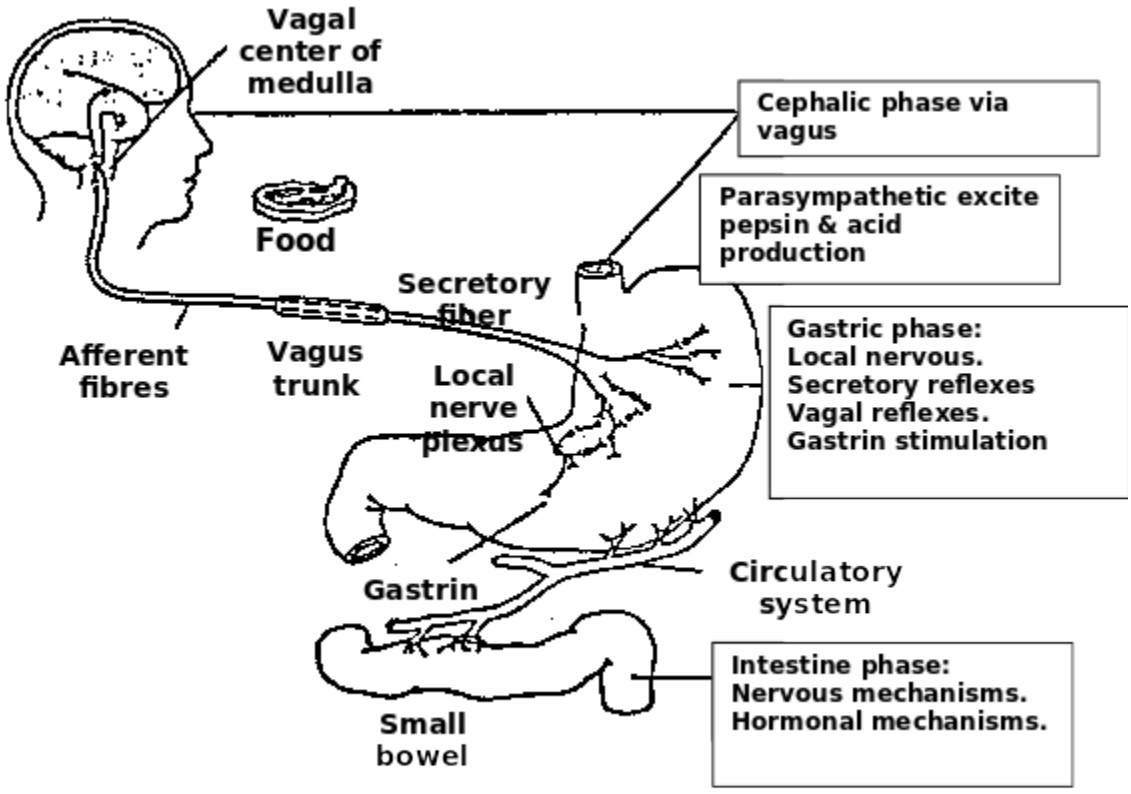

Fig. (2): The three phases of gastric secretion

(III) <u>The intestinal inhibitory phase: (Nervous and Horrnonal):</u>

This inhibitory phase results from the presence of food in the duodenum, which results in depression of gastric secretion by:

- Enterogastric reflex.

- Hormones which inhibit gastric secretion, such as GIF, VIP, CCK and secretin.

Mechanisms of inhibition of gastric secretion:

1. Drop of pH in the pyloric region and the duodenum, below 2 inhibits the secretion of gastrin i.e. **HCI inhibits its own secretion**.
2. Enterogastric reflex which occurs as a result of increased acid or distension of duodenum.
3. Presence of fat and hypertonic sugars in duodenum releases GIP, CCK, secretin and VIP.
4. Emotional depression and fear, via impulses from cerebral cortex, inhibit the dorsal vagal nucleus.
5. Somatostatin hormone which acts by **a paracrine manner**.

Mucosal Barrier:

In normal individuals the gastric mucosa does not become irritated or digested because of insoulible mucus ,mucus which is secreted by the surface mucous cells in the stomach, is made up of glycoproteins called mucins.

The mucus forms a flexible gel that coats the mucosa. HCI secreted by the parietal cells in the gastric glands crosses this barrier in finger like channels, leaving the rest of the gel layer intact.

The barrier is formed of:

- The insoluble mucus, which forms a gel like layer covering the mucous membrane.
- The integrity of the membrane of the mucosal cells: The membrane is impermeable to hydrogen ions and there is an active transport mechanism pumping H^+ ions from the mucosal cell into the gastric lumen, and Na^+ ions from the cells into the interstitial fluid.

Prosatglandins strengthen and augment the gastric mucosal barrier and stimulate mucus and bicarbonate secretion. They also inhibit acid secretion and increase mucosal blood flow.

-Substances that tend to disrupt the barrier and cause gastric irritation and ulcer include ethanol, vinegar, bile salts, aspirin, corticosteroids, and other nonsteroidal anti-inflammatory drugs. Aspirin and related drugs inhibit prostaglandin synthesis and consequently mucus secretion.

Peptic Ulcer:

The mucous membrane of the stomach is protected against the corrosive and digestive actions of HCl and pepsin by the gastric mucosal barrier.

Causes of peptic ulcers:

1- **Breakdown of the gastric mucosal barrier**

by various agents e.g.:

a. Alcohol.

b. Asprin, and non-steroidal inflammatory drugs; both inhibit the production of prostaglandins and consequently decrease mucus and HCO3- secretion.

c. Infection with specific bacteria called *Helicobacter pylori* which disrupts the mucosal barrier.

2-**Excess secretion of HCl**

In Zollinger-Ellison syndrome, there is excess secretion of gastrin hormone by tumors in the pancreas. Gastrin causes prolonged secretion of acid and severe ulcers.

As a result of breakdown of the barrier, H^+ ions diffuse from the gastric lumen to the cell, and Na^+ ions diffuse from the plasma to the cell. The increased concentrations of H^+ and Na^+ ions intracellularly destroy cellular metabolic function, and ulcers are formed in the mucosa.

Treatment of peptic ulcers:

Gastric and duodenal ulcers can be given a chance to heal by:

(1) Inhibition of acid secretion:

a) Blockage of H_2 histamine receptors on the parietal cells, e.g. by cimetidine.

b) Inhibit H^+-K+ ATPase in the apical membrane of parietal cells by proton pump inhibitors e.g. **Omeprazole.**

(2) Eradication of *Helicobacter pylori* with antibiotics.

(3) Stop use of aspirin and non-steroidal anti-inflammatory drugs.

(4) Surgical removal of gastrin-secreting tumors.